

10/034746
Search results
for Page # 8

WEST

Search Results -

Terms	Documents
L11 and combretastatin	0

Database:

US Patents Full-Text Database
US Pre-Grant Publication Full-Text Database
JPO Abstracts Database
EPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search:

L12

Search History

DATE: Tuesday, April 29, 2003 [Printable Copy](#) [Create Case](#)

Set Name Query
 side by side

Hit Count **Set Name**
 result set

DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR

<u>L12</u>	L11 and combretastatin	0	<u>L12</u>
<u>L11</u>	inhibit\$ near10 nitric near oxide near synthase near10 immun\$	47	<u>L11</u>
<u>L10</u>	nitric near oxide near synthase near10 immun\$	175	<u>L10</u>
<u>L9</u>	(combretastatin or CA near 4 near P) near10 immun\$	4	<u>L9</u>
<u>L8</u>	combretastatin near10 immun\$	4	<u>L8</u>
<u>L7</u>	L4 and (combretastatin or CA near 4 near P) near10 (enhance\$ or increase\$) near5 immune\$	2	<u>L7</u>
<u>L6</u>	L4 and (combretastatin or CA near 4 near P) near10 (enhance\$ or incresae\$) near5 immune\$	2	<u>L6</u>
<u>L5</u>	L4 and (enhance\$ or incresae\$) near5 immune\$	12	<u>L5</u>
<u>L4</u>	L3 and vascular	88	<u>L4</u>
<u>L3</u>	combretastatin\$ or CA near 4 near P or combretastatin near A4	209	<u>L3</u>
<u>L2</u>	L1 and vascular	7	<u>L2</u>
<u>L1</u>	combretastin or CA near 4 near p or combretastin near A4	19	<u>L1</u>

WEST[Help](#) [Logout](#) [Interrupt](#)[Main Menu](#) [Search Form](#) [Posting Counts](#) [Show S Numbers](#) [Edit S Numbers](#) [Preferences](#) [Cases](#)**Search Results -**

Terms	Documents
(combretastatin or CA near 4 near P) near10 immun\$	4

US Patents Full-Text Database
US Pre-Grant Publication Full-Text Database
JPO Abstracts Database
EPO Abstracts Database
Derwent World Patents Index
Database: IBM Technical Disclosure Bulletins

Search:

Your wildcard search against 10000 terms has yielded the results below.

The next term would be: ;

IMMUN\$(IMMUNO-SUPPRESANT).P66-P132,P133-P140,P61-P65,P57-P60,P35-P55,P56-P56.

Your result set for the last L# is incomplete.

The probable cause is use of unlimited truncation. Revise your search strategy to use limited truncation.

Search History

DATE: Tuesday, April 29, 2003 [Printable Copy](#) [Create Case](#)

Set Name Query
side by sideHit Count Set Name
result set

DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR

<u>L9</u>	(combretastatin or CA near 4 near P) near10 immun\$	4	<u>L9</u>
<u>L8</u>	combretastatin near10 immun\$	4	<u>L8</u>
<u>L7</u>	L4 and (combretastatin or CA near 4 near P) near10 (enhance\$ or increase\$) near5 immune\$	2	<u>L7</u>
<u>L6</u>	L4 and (combretastatin or CA near 4 near P) near10 (enhance\$ or incresaes\$) near5 immune\$	2	<u>L6</u>
<u>L5</u>	L4 and (enhance\$ or incresaes\$) near5 immune\$	12	<u>L5</u>
<u>L4</u>	L3 and vascular	88	<u>L4</u>
<u>L3</u>	combretastatin\$ or CA near 4 near P or combretastatin near A4	209	<u>L3</u>
<u>L2</u>	L1 and vascular	7	<u>L2</u>
<u>L1</u>	combretastin or CA near 4 near p or combretastin near A4	19	<u>L1</u>

END OF SEARCH HISTORY

WEST[Generate Collection](#)[Print](#)**Search Results - Record(s) 1 through 12 of 12 returned.**

1. Document ID: US 20030055014 A1

L5: Entry 1 of 12

File: PGPB

Mar 20, 2003

PGPUB-DOCUMENT-NUMBER: 20030055014

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030055014 A1

TITLE: Inhibition of angiogenesis by nucleic acids

PUBLICATION-DATE: March 20, 2003

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Bratzler, Robert L.

Concord

MA

US

US-CL-CURRENT: 514/44

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC
Draw Desc	Image										

2. Document ID: US 20020160973 A1

L5: Entry 2 of 12

File: PGPB

Oct 31, 2002

PGPUB-DOCUMENT-NUMBER: 20020160973

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020160973 A1

TITLE: Use of combretastatin A4 and its prodrugs as an immune enhancing therapy

PUBLICATION-DATE: October 31, 2002

INVENTOR-INFORMATION:

NAME

CITY

STATE

COUNTRY

RULE-47

Pero, Ronald W.

Sandgate

VT

US

Lee, Francis Y.F.

Yardley

PA

US

Edvardsen, Klaus

Lund

SE

Sjogren, Hans Olov

Lund

SE

US-CL-CURRENT: 514/44; 424/85.1, 514/12

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC
Draw Desc	Image										

3. Document ID: US 20020119153 A1

L5: Entry 3 of 12

File: PGPB

Aug 29, 2002

PGPUB-DOCUMENT-NUMBER: 20020119153
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020119153 A1

TITLE: Antibody conjugate formulations for selectively inhibiting VEGF

PUBLICATION-DATE: August 29, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Thorpe, Philip E.	Dallas	TX	US	
Brekken, Rolf A.	Seattle	WA	US	

US-CL-CURRENT: 424/145.1; 424/133.1, 530/388.24

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMPC
Draw Desc	Image										

4. Document ID: US 20020114809 A1

L5: Entry 4 of 12

File: PGPB

Aug 22, 2002

PGPUB-DOCUMENT-NUMBER: 20020114809
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020114809 A1

TITLE: Restore cancer-suppressing functions to neoplastic cells through DNA hypomethylation

PUBLICATION-DATE: August 22, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Rubinfeld, Joseph	Danville	CA	US	
Chang, Lucy	San Mateo	CA	US	
DiMartino, Jorge	San Carlos	CA	US	

US-CL-CURRENT: 424/155.1; 424/277.1, 424/649, 514/171, 514/183, 514/254.07, 514/269,
514/27, 514/283, 514/34, 514/49

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KMPC
Draw Desc	Image									

5. Document ID: US 6524583 B1

L5: Entry 5 of 12

File: USPT

Feb 25, 2003

US-PAT-NO: 6524583
DOCUMENT-IDENTIFIER: US 6524583 B1

TITLE: Antibody methods for selectively inhibiting VEGF

DATE-ISSUED: February 25, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Thorpe; Philip E.	Dallas	TX		
Brekken; Rolf A.	Seattle	WA		

US-CL-CURRENT: 424/145.1, 424/133.1, 424/135.1, 424/141.1, 530/387.1, 530/388.1,
530/388.15, 530/388.25, 530/809, 530/864, 530/865, 530/866

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

6. Document ID: US 6416758 B1

L5: Entry 6 of 12

File: USPT

Jul 9, 2002

US-PAT-NO: 6416758

DOCUMENT-IDENTIFIER: US 6416758 B1

**** See image for Certificate of Correction ****

TITLE: Antibody conjugate kits for selectively inhibiting VEGF

DATE-ISSUED: July 9, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Thorpe; Philip E.	Dallas	TX		
Brekken; Rolf A.	Seattle	WA		

US-CL-CURRENT: 424/145.1, 424/1.49, 424/1.53, 424/1.69, 424/133.1, 424/134.1,
424/135.1, 424/141.1, 424/142.1, 424/178.1, 424/179.1, 424/181.1, 424/183.1,
424/195.11, 424/9.2, 424/9.3, 435/69.1, 435/69.6, 435/69.7, 435/7.23, 435/70.21,
435/810, 530/387.3, 530/388.1, 530/388.15, 530/388.24, 530/391.3, 530/391.7,
530/391.9

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

7. Document ID: US 6406693 B1

L5: Entry 7 of 12

File: USPT

Jun 18, 2002

US-PAT-NO: 6406693

DOCUMENT-IDENTIFIER: US 6406693 B1

TITLE: Cancer treatment methods using antibodies to aminophospholipids

DATE-ISSUED: June 18, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Thorpe; Philip E.	Dallas	TX		
Ran; Sophia	Dallas	TX		

US-CL-CURRENT: 424/130.1, 424/132.1, 424/133.1, 424/135.1, 424/138.1, 424/141.1,
424/152.1, 424/184.1, 435/6, 530/387.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMC

 8. Document ID: US 6342221 B1

L5: Entry 8 of 12

File: USPT

Jan 29, 2002

US-PAT-NO: 6342221

DOCUMENT-IDENTIFIER: US 6342221 B1

**** See image for Certificate of Correction ****

TITLE: Antibody conjugate compositions for selectively inhibiting VEGF

DATE-ISSUED: January 29, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Thorpe; Philip E.	Dallas	TX		
Brekken; Rolf A.	Seattle	WA		

US-CL-CURRENT: 424/178.1, 424/1.49, 424/1.53, 424/130.1, 424/179.1, 424/181.1,
424/183.1, 424/193.1, 424/195.11, 424/9.3, 424/9.34, 424/9.6, 435/69.1, 435/7.1,
435/7.21, 435/7.23, 435/70.21, 435/810, 530/391.1, 530/391.3, 530/391.5, 530/391.7,
530/391.9

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMC

 9. Document ID: US 6342219 B1

L5: Entry 9 of 12

File: USPT

Jan 29, 2002

US-PAT-NO: 6342219

DOCUMENT-IDENTIFIER: US 6342219 B1

TITLE: Antibody compositions for selectively inhibiting VEGF

DATE-ISSUED: January 29, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Thorpe; Philip E.	Dallas	TX		
Brekken; Rolf A.	Seattle	WA		

US-CL-CURRENT: 424/145.1, 424/133.1, 424/134.1, 424/135.1, 424/141.1, 424/142.1,
424/143.1, 435/335, 435/69.1, 435/810, 530/387.1, 530/387.3, 530/388.1, 530/388.15,
530/388.23, 530/391.1, 530/391.3, 530/391.5, 530/391.7, 530/809, 530/864, 530/865,
530/866

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Draw Desc	Image								

KMC

 10. Document ID: US 6312694 B1

L5: Entry 10 of 12

File: USPT

Nov 6, 2001

US-PAT-NO: 6312694
 DOCUMENT-IDENTIFIER: US 6312694 B1
 ** See image for Certificate of Correction **

TITLE: Cancer treatment methods using therapeutic conjugates that bind to aminophospholipids

DATE-ISSUED: November 6, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Thorpe; Philip E.	Dallas	TX		
Ran; Sophia	Dallas	TX		

US-CL-CURRENT: 424/178.1, 424/133.1, 424/134.1, 424/135.1, 424/136.1, 424/137.1,
424/141.1, 424/142.1, 424/143.1, 424/181.1, 424/193.1, 514/12, 530/387.1, 530/388.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Drawn Desc	Image								

KM/C

11. Document ID: WO 2058535 A2

L5: Entry 11 of 12

File: EPAB

Aug 1, 2002

PUB-NO: WO002058535A2

DOCUMENT-IDENTIFIER: WO 2058535 A2

TITLE: USE OF COMBRETASTATIN A4 AND ITS PRODRUGS AS AN IMMUNE ENHANCING THERAPY

PUBN-DATE: August 1, 2002

INVENTOR-INFORMATION:

NAME	COUNTRY
PERO, RONALD W	
LEE, FRANCIS Y F	
EDVARDSEN, KLAUS	
SJOEGREN, HANS OLOV	

INT-CL (IPC): A61 B 0/

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
Drawn Desc	Image								

KM/C

12. Document ID: WO 200258535 A2 US 20020160973 A1

L5: Entry 12 of 12

File: DWPI

Aug 1, 2002

DERWENT-ACC-NO: 2002-732689

DERWENT-WEEK: 200279

COPYRIGHT 2003 DERWENT INFORMATION LTD

TITLE: Use of combretastatin A4 and/or its prodrugs as an immune enhancing therapy for treating immunosuppression

INVENTOR: EDVARDSEN, K; LEE, F Y F ; PERO, R W ; SJOEGREN, H O ; SJOEGREN, H O

PRIORITY-DATA: 2000US-258283P (December 26, 2000), 2001US-0034746 (December 26,

, 2001)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200258535 A2	August 1, 2002	E	046	A61B000/00
US 20020160973 A1	October 31, 2002		000	A61K048/00

INT-CL (IPC) : A61 B 0/00; A61 K 38/17; A61 K 38/19; A61 K 48/00

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#) | [KMC](#) |
[Draw Desc](#) | [Image](#) |

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Terms	Documents
L4 and (enhance\$ or incresae\$) near5 immune\$	12

Display Format:

[Previous Page](#) [Next Page](#)

set hi ;**set hi**
HIGHLIGHT set on as ''
HIGHLIGHT set on as ''
? begin 5,6,55,154,155,156,312,399,biotech,biosci
>>> 135 is unauthorized

Set Items Description

? s combretastatin? and immun?
>>>File 5 processing for IMMUN? stopped at IMMUNODEPRESSED
>>>File 55 processing for IMMUN? stopped at IMMUNOGENICITYOF
>>>File 154 processing for IMMUN? stopped at IMMUNOFLOW
>>>File 155 processing for IMMUN? stopped at IMMUNOCLUSTERED
>>>File 156 processing for IMMUN? stopped at IMMUNOPOTENTIATOR
>>>File 399 processing for IMMUN? stopped at IMMUNOMUDALATORY
Processing
>>>File 34 processing for IMMUN? stopped at IMMUNOFLURESCENCE
Processed 10 of 34 files ...
>>>File 71 processing for IMMUN? stopped at IMMUNORECTIVITY
>>>File 73 processing for IMMUN? stopped at IMMUNOCOMPROMISING
>>>File 144 processing for IMMUN? stopped at IMMUNODENSITY
Processing
Processed 20 of 34 files ...
>>>File 50 processing for IMMUN? stopped at IMMUNOPRECIPITATING
Completed processing all files
 1905 COMBRETASTATIN?
 6393344 IMMUN?
 S1 76 COMBRETASTATIN? AND IMMUN?
? s s1 and immunosuppression
 76 S1
 212188 IMMUNOSUPPRESSION
 S2 0 S1 AND IMMUNOSUPPRESSION
? s combretastatin? and immunosuppression
 1905 COMBRETASTATIN?
 212188 IMMUNOSUPPRESSION
 S3 0 COMBRETASTATIN? AND IMMUNOSUPPRESSION
? s combretastatin? and immunotherapy?
 1905 COMBRETASTATIN?
 273232 IMMUNOTHERAP?
 S4 12 COMBRETASTATIN? AND IMMUNOTHERAP?
? rd s4
...completed examining records
 S5 8 RD S4 (unique items)
? d s5/9/1-8
 Display 5/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

11877151 BIOSIS NO.: 199900123260
Immunotherapy combined with antiangiogenic drugs.
AUTHOR: Sjogren Hans O(a)
AUTHOR ADDRESS: (a)Tumor Immunol. Unit, CMB, Wallenberg Lab., Univ. Lund,
Lund**Sweden
JOURNAL: Tumor Biology 19 (SUPPL. 2):p5 Aug., 1998
CONFERENCE/MEETING: 26th Meeting of the International Society for
Oncodevelopmental Biology and Medicine Umea, Sweden August 30-September
4, 1998
ISSN: 1010-4283
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 82855-09-2: COMBRETASTATIN; 86090-08-6: ANGIOSTATIN
DESCRIPTORS:
 MAJOR CONCEPTS: Immune System (Chemical Coordination and Homeostasis);
 Pharmacology; Tumor Biology

-more-

?
 Display 5/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

(c) 2003 BIOSIS. All rts. reserv.
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: rat (Muridae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
DISEASES: colon carcinoma--digestive system disease, neoplastic disease
CHEMICALS & BIOCHEMICALS: angiostatin--antiangiogenic; combretastatin--antiangiogenic
MISCELLANEOUS TERMS: immunotherapy; Meeting Abstract
ALTERNATE INDEXING: Carcinoma (MeSH); Colonic Neoplasms (MeSH)
CONCEPT CODES:
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy
12512 Pathology, General and Miscellaneous-Therapy (1971-)
14006 Digestive System-Pathology
14508 Cardiovascular System-Blood Vessel Pathology
22010 Pharmacology-Cardiovascular System
34502 Immunology and Immunochemistry-General; Methods

-more-

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Display 5/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
10060 Biochemical Studies-General
BIOSYSTEMATIC CODES:
86375 Muridae

- end of record -

?
Display 5/9/2 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 2003 American Chemical Society. All rts. reserv.

137119643 CA: 137(9)119643z PATENT
Methods using a combretastatin compound combined with an antitumor agent for modulating tumor growth and metastasis
INVENTOR(AUTHOR): Lee, Francis Y.; Peck, Ronald; Chaplin, David; Pero, Ronald; Edvardsen, Klaus
LOCATION: USA
ASSIGNEE: Bristol-Myers Squibb Company; Oxigene, Inc.
PATENT: PCT International ; WO 200256692 A1 DATE: 20020725
APPLICATION: WO 2001US50261 (20011220) *US PV258195 (20001222)
PAGES: 69 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A01N-057/00A;
A61K-038/00B DESIGNATED COUNTRIES: AE; AG; AL; AM; AT; AU; AZ; BA; BB; BG;
BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DZ; EC; EE; ES; FI; GB;
GD; GE; GH; GM; HR; HU; ID; IL; IN; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR;
LS; LT; LU; LV; MA; MD; MG; MK; MN; MW; MX; MZ; NO; NZ; OM; PH; PL; PT; RO;
RU; SD; SE; SG; SI; SK; SL; TJ; TM; TN; TR; TT; TZ; UA; UG; US; UZ; VN; YU;
ZA; ZM; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM

-more-

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Display 5/9/2 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)
(c) 2003 American Chemical Society. All rts. reserv.
; KE; LS; MW; MZ; SD; SL; SZ; TZ; UG; ZM; ZW; AT; BE; CH; CY; DE; DK; ES;
FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; TR; BF; BJ; CF; CG; CI; CM; GA;
GN; GQ; GW; ML; MR; NE; SN; TD; TG
SECTION:
CA201006 Pharmacology

CA263XXX Pharmaceuticals

IDENTIFIERS: combretastatin compd antitumor agent combination neoplasm metastasis treatment

DESCRIPTORS:

Nutrients...

anti-; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Antitumor agents...

antibiotic; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Estrogens...

antiestrogens; combretastatin compd. combined with antitumor agent for

-more-

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Display 5/9/2 (Item 1 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

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modulating tumor growth and metastasis

Antibiotics...

antitumor; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Pseudomonas...

BR96-sFv-PE40 immunoconjugate; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Mammary gland... Ovary, neoplasm...

carcinoma; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Intestine, neoplasm...

colon; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Alkylating agents, biological... Antitumor agents... Circulation... Drug delivery systems... Drug interactions... Human... Immunotherapy... Neoplasm... Pharmacokinetics... Radiotherapy... Taxanes...
combretastatin compd. combined with antitumor agent for modulating

-more-

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Display 5/9/2 (Item 1 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

(c) 2003 American Chemical Society. All rts. reserv.
tumor growth and metastasis

Toxins...

exotoxins, BR96-sFv-PE40 immunoconjugate; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Sarcoma...

fibrosarcoma; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Drug delivery systems...

immunotoxins; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Neoplasm...

metastasis; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Mitosis...

mitotic inhibitors; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

-more-

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Display 5/9/2 (Item 1 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

(c) 2003 American Chemical Society. All rts. reserv.
Antibodies...

monoclonal, conjugates, BR96-sFv-PE40 immunoconjugate; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Mammary gland...

neoplasm; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Drug delivery systems...

prodrugs; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

Drug interactions...

synergistic; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

CAS REGISTRY NUMBERS:

50-07-7 50-18-0 50-76-0 51-21-8 51-75-2 57-22-7 58-05-9 59-05-2
147-94-4 148-82-3 154-93-8 305-03-3 595-33-5 865-21-4 3778-73-2
4342-03-4 11056-06-7 13010-47-4 15663-27-1 20830-81-3 21679-14-1

-more-

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Display 5/9/2 (Item 1 from file: 399)
DIALOG(R) File 399:CA SEARCH(R)

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23214-92-8 25316-40-9 33069-62-4 33419-42-0 41575-94-4 58957-92-9
61825-94-3 71486-22-1 74381-53-6 74578-38-4 95058-81-4 100286-90-6
107868-30-4 109971-63-3 114977-28-5 117048-59-6 117091-64-2
120511-73-1 121584-18-7 123948-87-8 146426-40-6 168555-66-6
180288-69-1 184475-35-2 252916-29-3 288847-34-7 443913-73-3

combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

13010-20-3D 109971-63-3D 117048-59-6D derivs., combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

143180-75-0 inhibitors; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

9039-48-9 nonsteroidal inhibitors; combretastatin compd. combined with antitumor agent for modulating tumor growth and metastasis

- end of record -

?

Display 5/9/3 (Item 1 from file: 8)

DIALOG(R) File 8:EI Compendex(R)

(c) 2003 Elsevier Eng. Info. Inc. All rts. reserv.

05339745 E.I. No: EIP99084755247

Title: Examples of adjuvant treatment enhancing the antitumor effect of photodynamic therapy

Author: Korbelik, Mladen; Cecic, Ivana; Sun, Jinghai; Chaplin, David J.

Corporate Source: British Columbia Cancer Agency, Vancouver, BC, Can

Conference Title: Proceedings of the 1999 Optical Methods for Tumor Treatment and Detection: Mechanisms and Techniques in Photodynamic Therapy VIII

Conference Location: San Jose, CA, USA Conference Date:
19990123-19990124

Sponsor: SPIE; IBOS

E.I. Conference No.: 55251

Source: Proceedings of SPIE - The International Society for Optical Engineering v 3592 1999. p 65-72

Publication Year: 1999

CODEN: PSISDG ISSN: 0277-786X

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Display 5/9/3 (Item 1 from file: 8)
DIALOG(R)File 8:Ei Compendex(R)
(c) 2003 Elsevier Eng. Info. Inc. All rts. reserv.
Language: English
Document Type: JA; (Journal Article) Treatment: L; (Literature Review/Bibliography); X; (Experimental)
Journal Announcement: 9909W5

Abstract: Strategies for improving the clinical efficacy of photodynamic therapy (PDT) in treatment of solid cancers include applications of different types of adjuvant treatments in addition to this modality that may result in superior therapeutic outcome. Examples of such an approach investigated using mouse tumor models are presented in this report. It is shown that the cures of PDT treated subcutaneous tumors can be substantially improved by adjuvant therapy with: metoclopramide (enhancement of cancer cell apoptosis), **combretastatin** A-4 (selective destruction of tumor neovasculature), Roussin's Black Salt (light activated tumor localized release of nitric oxide), or dendritic cell-based adoptive **immunotherapy** (immune rejection of treated tumor). (Author abstract)

51 Refs.

Descriptors: *Photodynamic therapy; Oncology; Immunology

-more-

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Display 5/9/3 (Item 1 from file: 8)
DIALOG(R)File 8:Ei Compendex(R)
(c) 2003 Elsevier Eng. Info. Inc. All rts. reserv.
Identifiers: Antitumor effects; Roussin's black salt
Classification Codes:
461.9.1 (Immunology)
461.6 (Medicine); 741.1 (Light/Optics); 461.9 (Biology)
461 (Biotechnology); 741 (Optics & Optical Devices)
46 (BIOENGINEERING); 74 (OPTICAL TECHNOLOGY)

- end of record -

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Display 5/9/4 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

01808445 2001170229
Eradication of colorectal xenografts by combined radioimmunotherapy and **combretastatin** A-4 3-O-phosphate
Pedley R.B.; Hill S.A.; Boxer G.M.; Flynn A.A.; Boden R.; Watson R.; Dearling J.; Chaplin D.J.; Begent R.H.J.
ADDRESS: R.B. Pedley, Department of Oncology, Royal Free and Univ. Coll.
Med. Sch., Royal Free Campus, Rowland Hill Street, London NW3 2PF
, United Kingdom
Journal: Cancer Research, 61/12 (4716-4722), 2001, United States
PUBLICATION DATE: June 15, 2001
CODEN: CNREA
ISSN: 0008-5472
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 33

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Display 5/9/4 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
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Solid tumors have a heterogeneous pathophysiology, which has a major impact on therapy. Using SW1222 colorectal xenografts grown in nude mice, we have

shown that antibody-targeted radioimmunotherapy (RIT) effectively treated the well-perfused tumor rim, producing regressions for (similar) 35 days, but was less effective at the more hypoxic center. By 72 h after RIT, the number of apoptotic cells rose from an overall value of 1% in untreated tumors to 35% at the tumor periphery and 10% at the center. The antivascular agent disodium **combretastatin** A-4 3-O-phosphate (CA4-P) rapidly reduced tumor blood flow to 62% of control values by 1 h, 23% by 3 h, and between 32-36% from 6 to 24 h after administration. This created central hemorrhagic necrosis, but a peripheral rim of cells continued to grow, and survival was unaffected. Changes in the pattern of perfusion across the tumor over time were zonal. Untreated mice showed perfusion throughout the tumor, with greatest activity at the rim. There was an overall reduction at 1 h, and total cessation of central perfusion from 3 h onward. A narrow peripheral rim of perfusion was always present, which increased in intensity and extent between 6 and 24 h, either through

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reperfusion or new vessel growth. Combining these two complementary therapies (7.4 MBq SUP131I-labeled anti-carcinoembryonic antigen IgG i.v. plus a single 200 mg/kg dose of CA4-P i.p.) produced complete cures in five of six mice for >9 months. Allowing maximal tumor localization of antibody (48 h) before blood flow inhibition by CA4-P increased tumor retention by two to three times control levels by 96 h without altering normal tissue levels, as confirmed by gamma counting and phosphor image analysis. The success of this combined, synergistic therapy was probably the result of several factors: (a) the killing of tumor cells in the outer, radiosensitive region by targeted radiotherapy; (b) enhancement of RIT by entrapment of additional radioantibody after **combretastatin**-induced vessel collapse; and (c) destruction of the central, more hypoxic and radioresistant region by CA4-P. This work demonstrates the need to consider cancer treatment in a biologically heterogeneous setting, if results are to be effectively translated to the clinic.

CLASSIFICATION CODE AND DESCRIPTION:

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Display 5/9/4 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.
87.4.2 - CANCER RESEARCH / TREATMENT / Radiotherapy
87.4.3 - CANCER RESEARCH / TREATMENT / **Immunotherapy**
87.4.11 - CANCER RESEARCH / TREATMENT / Treatment Monitoring and Evaluation
86.9.2 - IMMUNOLOGY AND INFECTIOUS DISEASES / TUMOUR IMMUNOLOGY / Immune Response

- end of record -

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Display 5/9/5 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

11796913 EMBASE No: 2002367661
Potential of DMXAA combination therapy for solid tumors
Baguley B.C.; Wilson W.R.
B.C. Baguley, Auckland Cancer Society Res. Centre, The University of Auckland, Auckland New Zealand
AUTHOR EMAIL: b.baguley@auckland.ac.nz
Expert Review of Anticancer Therapy (EXPERT REV. ANTICANCER THER.) (

United Kingdom) 2002, 2/5 (593-603)
CODEN: ERATB ISSN: 1473-7140
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 84

DMXAA is one of the first examples of a new class of anticancer agents that attack existing tumor blood vessels and thus deprives tumor tissue of an adequate blood supply. Its mechanism of action appears to rely on the

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Induction within tumor tissue of cytokines, such as tumor necrosis factor. In experimental tumors, DMXAA interacts productively with radiation, hyperthermia and a number of chemotherapeutic drugs. This review discusses the mechanisms underlying such interactions and how these might be exploited in clinical cancer treatment.

BRAND NAME/MANUFACTURER NAME: sr 4233

DRUG DESCRIPTORS:

*5,6 dimethylxanthene 4 acetic acid--adverse drug reaction--ae; *5,6 dimethylxanthene 4 acetic acid--clinical trial--ct; *5,6 dimethylxanthene 4 acetic acid--drug analysis--an; *5,6 dimethylxanthene 4 acetic acid--drug combination--cb; *5,6 dimethylxanthene 4 acetic acid--drug interaction--it; *5,6 dimethylxanthene 4 acetic acid--drug therapy--dt; *5,6 dimethylxanthene 4 acetic acid--drug toxicity--to; *5,6 dimethylxanthene 4 acetic acid--pharmacology--pd
antineoplastic agent--adverse drug reaction--ae; antineoplastic agent

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DIALOG(R) File 73:EMBASE
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--clinical trial--ct; antineoplastic agent--drug analysis--an;
antineoplastic agent--drug combination--cb; antineoplastic agent--drug interaction--it; antineoplastic agent--drug therapy--dt; antineoplastic agent--drug toxicity--to; antineoplastic agent--pharmacology--pd; cytokine --endogenous compound--ec; tumor necrosis factor--endogenous compound--ec; mitoflaxone--drug analysis--an; mitoflaxone--drug therapy--dt; mitoflaxone --pharmacology--pd; antiinflammatory agent--drug analysis--an;
antiinflammatory agent--drug therapy--dt; antiinflammatory agent --pharmacology--pd; xanthone 4 acetic acid--drug analysis--an; xanthone 4 acetic acid--drug therapy--dt; xanthone 4 acetic acid--pharmacology--pd;
colchicine--pharmacology--pd; vinblastine--pharmacology--pd;
combretastatin A4--clinical trial--ct; **combretastatin** A4--drug therapy--dt; 5 hydroxyindoleacetic acid--endogenous compound--ec; endotoxin --endogenous compound--ec; 1,2,3 benzotriazine derivative--clinical trial --ct; 1,2,3 benzotriazine derivative--drug combination--cb; 1,2,3 benzotriazine derivative--drug interaction--it; 1,2,3 benzotriazine derivative--drug therapy--dt; tirapazamine--clinical trial--ct;

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Display 5/9/5 (Item 1 from file: 73)
DIALOG(R) File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.
tirapazamine--drug interaction--it; tirapazamine--drug therapy--dt; 1,4 bis[[2 (dimethylamino n oxide)ethyl]amino] 5,8 dihydroxyanthraquinone

--clinical trial--ct; 1,4 bis[[2 (dimethylamino n oxide)ethyl]amino] 5,8 dihydroxyanthraquinone--drug combination--cb; 1,4 bis[[2 (dimethylamino n oxide)ethyl]amino] 5,8 dihydroxyanthraquinone--drug interaction--it; 1,4 bis[[2 (dimethylamino n oxide)ethyl]amino] 5,8 dihydroxyanthraquinone--drug therapy--dt; benzamide derivative--drug combination--cb; benzamide derivative--drug interaction--it; benzamide derivative--drug therapy--dt; benzamide derivative--pharmacology--pd; cytotoxic agent--drug combination --cb; cytotoxic agent--drug interaction--it; cytotoxic agent--drug therapy --dt; cytotoxic agent--drug toxicity--to; cytotoxic agent--pharmacokinetics --pk; cytotoxic agent--pharmacology--pd; melphalan--drug combination--cb; melphalan--drug interaction--it; melphalan--drug therapy--dt; melphalan --drug toxicity--to; melphalan--pharmacokinetics--pk; melphalan --pharmacology--pd; paclitaxel--drug combination--cb; paclitaxel--drug interaction--it; paclitaxel--drug therapy--dt; paclitaxel--pharmacokinetics --pk; paclitaxel--pharmacology--pd; docetaxel--drug combination--cb;

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DIALOG(R) File 73:EMBASE

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docetaxel--drug interaction--it; docetaxel--drug therapy--dt; docetaxel --pharmacology--pd; vincristine--drug combination--cb; vincristine--drug interaction--it; vincristine--drug therapy--dt; vincristine--pharmacology --pd; etoposide--drug combination--cb; etoposide--drug interaction--it; etoposide--drug therapy--dt; etoposide--pharmacology--pd; carboplatin--drug combination--cb; carboplatin--drug interaction--it; carboplatin--drug therapy--dt; carboplatin--pharmacokinetics--pk; carboplatin--pharmacology --pd; cyclophosphamide--drug combination--cb; cyclophosphamide--drug interaction--it; cyclophosphamide--drug therapy--dt; cyclophosphamide --pharmacology--pd; doxorubicin--drug combination--cb; doxorubicin--drug interaction--it; doxorubicin--drug therapy--dt; doxorubicin--pharmacology --pd; cisplatin--drug combination--cb; cisplatin--drug interaction--it; cisplatin--drug therapy--dt; cisplatin--pharmacology--pd; fluorouracil --drug combination--cb; fluorouracil--drug interaction--it; fluorouracil --drug therapy--dt; fluorouracil--pharmacology--pd; angiogenesis inhibitor --drug combination--cb; angiogenesis inhibitor--drug interaction--it; angiogenesis inhibitor--drug therapy--dt; angiogenesis inhibitor

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DIALOG(R) File 73:EMBASE

(c) 2003 Elsevier Science B.V. All rts. reserv.
--pharmacology--pd; thalidomide--drug combination--cb; thalidomide--drug interaction--it; thalidomide--drug therapy--dt; thalidomide--pharmacology --pd; unindexed drug

MEDICAL DESCRIPTORS:

*solid tumor--drug therapy--dt; *solid tumor--radiotherapy--rt
drug classification; tumor vascularization; cancer tissue; drug mechanism;
experimental neoplasm--drug therapy--dt; cancer radiotherapy; hyperthermia;
cancer chemotherapy; drug structure; drug activity; side effect--side
effect--si; drug potentiation; drug blood level; area under the curve; drug
tolerability; radioimmunotherapy; gene therapy; cancer **immunotherapy**;
human; nonhuman; clinical trial; controlled study; review
CAS REGISTRY NO.: 87626-55-9 (mitoflaxone); 64-86-8 (colchicine); 865-21-4
(vinblastine); 117048-59-6 (**combretastatin A4**); 1321-73-9,
54-16-0 (5 hydroxyindoleacetic acid); 27314-97-2 (tirapazamine);
136470-65-0 (1,4 bis[[2 (dimethylamino n oxide)ethyl]amino] 5,8
dihydroxyanthraquinone); 148-82-3 (melphalan); 33069-62-4 (paclitaxel);
114977-28-5 (docetaxel); 57-22-7 (vincristine); 33419-42-0 (etoposide);

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Display 5/9/5 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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41575-94-4 (carboplatin); 50-18-0 (cyclophosphamide); 23214-92-8,
25316-40-9 (doxorubicin); 15663-27-1, 26035-31-4, 96081-74-2 (cisplatin
); 51-21-8 (fluorouracil); 50-35-1 (thalidomide

SECTION HEADINGS:

- 014 Radiology
- 016 Cancer
- 030 Clinical and Experimental Pharmacology
- 037 Drug Literature Index
- 038 Adverse Reaction Titles

- end of record -

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Display 5/9/6 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

11445087 EMBASE No: 2002016166

From biology to therapy
VON DER BIOLOGIE ZUR THERAPIE
Azemar M.; Hildenbrand B.
Dr. M. Azemar, Klinik fur Tumorbioologie, Albert-Ludwigs-Universitat
Freiburg, Hugstetter Strasse 55, 79106 Freiburg Germany
Klinikarzt (KLINIKARTZ) (Germany) 2001, 30/12 (322-327)
CODEN: KLINF ISSN: 0341-2350
DOCUMENT TYPE: Journal ; Review
LANGUAGE: GERMAN SUMMARY LANGUAGE: ENGLISH; GERMAN

Metastases remain the main cause of death from solid tumours, the most common neoplasias. The initial successes of chemotherapies achieved in the middle of the 20th century were followed by years of disappointment and frustration. The present article describes the major steps in the development and metastasization of tumours on the basis of the latest

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results of relevant research. Also discussed are new therapeutic options based on the latest data. These include antiangiogenesis, antisense oligonucleotides, signal transduction inhibitors, and **immunotherapeutic** approaches. Many of these experimental treatment strategies are currently in advanced stages of clinical development, and will supplement established therapeutic options in future.

BRAND NAME/MANUFACTURER NAME: im 842; tnp 470; ae 941; su 5416; su 6668; ptk 787; zk 222584; g 3139; isis 3521; isis 5132; isis 2503; mg 98; apc 8015; qs 21

DRUG DESCRIPTORS:

marimastat; ae 941; fumagillool chloroacetylcarbamate; thalidomide; squalamine; **combretastatin** A4; endostatin; su 6668; 1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine; vasculotropin antibody; alpha interferon; monoclonal antibody lm 609; tetrathiomolybdic acid; antineoplastic agent; g 3139; isis 3521; cgp 69846a; isis 2503; gene expression modulator 231; antisense oligonucleotide; granulocyte macrophage

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Display 5/9/6 (Item 2 from file: 73)

DIALOG(R) File 73:EMBASE

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colony stimulating factor--clinical trial--ct; glycoprotein gp 100
--clinical trial--ct; qs 21--clinical trial--ct; glycoprotein gp 96
--clinical trial--ct; melan A--clinical trial--ct; unclassified drug; 3
[(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h indol 2 one

MEDICAL DESCRIPTORS:

*metastasis

pathogenesis; angiogenesis; molecular biology; malignant transformation;
signal transduction; cancer **immunotherapy**; drug efficacy; cancer
research; human; major clinical study; clinical trial; review

DRUG TERMS (UNCONTROLLED): 3 [(4,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3
dihydro 2h indol 2 one; im 842; mg 98; apc 8015--clinical trial--ct

CAS REGISTRY NO.: 154039-60-8 (marimastat); 129298-91-5 (fumagillo
chloroacetylcarbamate); 50-35-1 (thalidomide); 148717-90-2, 160022-48-0
(squalamine); 117048-59-6 (**combretastatin** A4); 187888-07-9 (endostatin);
252916-29-3 (su 6668); 212142-18-2 (1 (4 chloroanilino) 4 (4 pyridylmethyl)phthalazine); 13718-35-9, 16330-92-0 (tetrathiomolybdic acid); 190977-41-4 (g 3139); 151879-73-1 (isis 3521);

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Display 5/9/6 (Item 2 from file: 73)

DIALOG(R) File 73:EMBASE

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177075-18-2 (cgp 69846a); 149957-14-2 (isis 2503); 141256-04-4 (qs 21);
186610-95-7 (3 [(3,5 dimethyl 1h pyrrol 2 yl)methylene] 1,3 dihydro 2h
indol 2 one

SECTION HEADINGS:

016 Cancer

037 Drug Literature Index

- end of record -

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Display 5/9/7 (Item 3 from file: 73)

DIALOG(R) File 73:EMBASE

(c) 2003 Elsevier Science B.V. All rts. reserv.

10784849 EMBASE No: 2000261387

Canadian sarcoma group workshop sarcomas: Molecular markers to
therapeutics, 26-27 February 2000, Toronto, Canada

Bramwell V.; Andrulis I.; Bell R.; Eisenhauer E.; Fornasier V.; Kandel R.
; O'Sullivan B.; Temple W.; Turcotte R.; Wunder J.

V. Bramwell, London Regional Cancer Centre, 790 Commissioners Road East,
London, Ont. N6A 4L6 Canada

Sarcoma (SARCOMA) (United Kingdom) 2000, 4/1-2 (67-73)

CODEN: SARCF ISSN: 1357-714X

DOCUMENT TYPE: Journal; Conference Paper

LANGUAGE: ENGLISH

BRAND NAME/MANUFACTURER NAME: et 743; bbr 3464; ptk 787

DRUG DESCRIPTORS:

*irinotecan--clinical trial--ct; *irinotecan--drug therapy--dt; *ecteinascidin 743--clinical trial--ct; *ecteinascidin 743--drug therapy--dt
; *anthraquinone derivative--clinical trial--ct; *anthraquinone derivative

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Display 5/9/7 (Item 3 from file: 73)

DIALOG(R) File 73:EMBASE

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--drug therapy--dt; *DNA topoisomerase inhibitor--clinical trial--ct; *DNA
topoisomerase inhibitor--drug combination--cb; *DNA topoisomerase inhibitor
--drug interaction--it; *DNA topoisomerase inhibitor--drug therapy--dt

cisplatin--drug combination--cb; cisplatin--drug interaction--it; cisplatin--drug therapy--dt; cyclophosphamide--drug combination--cb; cyclophosphamide--drug interaction--it; cyclophosphamide--drug therapy--dt; bbr 3464--clinical trial--ct; bbr 3464--drug therapy--dt; **combretastatin A4**--clinical trial--ct; **combretastatin A4**--drug therapy--dt; unclassified drug

MEDICAL DESCRIPTORS:

*sarcoma--diagnosis--di; *sarcoma--drug therapy--dt; *sarcoma--epidemiology--ep; *sarcoma--radiotherapy--rt; *sarcoma--surgery--su; *soft tissue sarcoma--diagnosis--di; *soft tissue sarcoma--drug therapy--dt; *soft tissue sarcoma--epidemiology--ep; *soft tissue sarcoma--radiotherapy--rt; *soft tissue sarcoma--surgery--su molecular biology; cancer cytodiagnosis; cancer **immunotherapy**; quality of life; human; clinical trial; phase 2 clinical trial; human

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Display 5/9/7 (Item 3 from file: 73)

DIALOG(R)File 73:EMBASE

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tissue; human cell; conference paper; priority journal

DRUG TERMS (UNCONTROLLED): ptk 787--drug analysis--an; ptk 787--drug development--dv

CAS REGISTRY NO.: 100286-90-6 (irinotecan); 114899-77-3 (ecteinascidin 743); 15663-27-1, 26035-31-4, 96081-74-2 (cisplatin); 50-18-0 (cyclophosphamide); 172903-07-0 (bbr 3464); 117048-59-6 (**combretastatin A4**)

SECTION HEADINGS:

016 Cancer

037 Drug Literature Index

- end of record -

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Display 5/9/8 (Item 1 from file: 266)

DIALOG(R)File 266:FEDRIP

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00310425

IDENTIFYING NO.: 1R43CA88583-01A1 AGENCY CODE: CRISP

Potent Monoclonal Antibody Drug Conjugates

PRINCIPAL INVESTIGATOR: SENTER, PETER D

ADDRESS: SEATTLE GENETICS INC 21823 30TH DR. SE BOTHELL, WA 98021

PERFORMING ORG.: SEATTLE GENETICS, INC., BOTHELL, WASHINGTON

SPONSORING ORG.: NATIONAL CANCER INSTITUTE

FY : 2001 TYPE OF AWARD: New Award (Type 1)

SUMMARY: Phase I and II clinical trials with BR96-doxorubicin, an immunoconjugate that recognizes receptors on human carcinomas, have demonstrated that the monoclonal antibody component, BR96, is capable of safely delivering active doxorubicin to tumor masses, albeit at concentrations that are sub-optimal. We propose to construct and test significantly improved conjugates consisting of highly potent drugs attached to BR96 through a new generation of optimized peptide-based linkers. The resulting conjugates should be stable in serum, but labile

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DIALOG(R)File 266:FEDRIP

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inside tumor cell lysosomes, leading to the release of active drug at the target site. The drugs will consist of two classes. Minor groove binders containing a distamycin unit will be attached to the DNA alkylator cyclopropylpyrroloindole, forming a construct that will covalently modify

the DNA of target cancer cells. The second drug will be **combreastatin A4**, a potent antimitotic agent that acts both on tumor cells and tumor vasculature. It is expected that conditionally stable conjugates prepared with these agents will be potent and capable of effecting antitumor activities at biologically relevant doses. The aims of the proposed study are to synthesize potent drug derivatives, link them to BR96 and to a monoclonal antibody against the CD40 antigen, and evaluate their stability characteristics in vitro cytotoxic activities, and in vivo toxicities and activities in nude mice with human tumor xenografts.

PROPOSED COMMERCIAL APPLICATIONS: There is a very large unmet clinical need for treating carcinomas of the breast, lung, colon, and prostate. The BR96 antibody recognizes the Lewis-Y antigen, which is widely expressed on these tumors. Using the BR96 antibody for the delivery of potent drugs to

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Display 5/9/8 (Item 1 from file: 266)
DIALOG(R) File 266:FEDRIP
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tumors may lead to pronounced anticancer activity with acceptable levels of systemic toxicity. This would constitute a major advancement in the clinical treatment of cancer.

DESCRIPTORS: athymic mouse; antimitotic; antineoplastic; lysosome; chemical conjugate; immunoconjugate; monoclonal antibody; immunopharmacology; neoplasm /cancer **immunotherapy**; antitumor antibody; lung neoplasm; neoplasm /cancer pharmacology; high performance liquid chromatography; cathepsin B; nonhuman therapy evaluation; SDS polyacrylamide gel electrophoresis; cell line; enzyme activity; angiogenesis inhibitor

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? s combreastatin? and nitric (n) oxide
Processed 30 of 34 files ...
Processing
Completed processing all files
 1905 COMBREASTATIN?
 655754 NITRIC
 2943712 OXIDE
 575988 NITRIC(N)OXIDE
 S6 61 COMBREASTATIN? AND NITRIC (N) OXIDE
? s s6 and synthase
 61 S6
 630955 SYNTHASE
 S7 41 S6 AND SYNTHASE
? rd s7
...completed examining records
 S8 10 RD S7 (unique items)
? d s8/3/1-10
 Display 8/3/1 (Item 1 from file: 5)
DIALOG(R) File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

14159823 BIOSIS NO.: 200300153852

The First International Conference on Vascular Targeting: Meeting overview.

AUTHOR: Thorpe Philip E(a); Chaplin David J; Blakey David C

AUTHOR ADDRESS: (a)Department of Pharmacology, University of Texas
Southwestern Medical Center, Dallas, TX, 75390, USA**USA E-Mail:
philip.thorpe@utsouthwestern.edu

JOURNAL: Cancer Research 63 (5):p1144-1147 March 1 2003 2003

MEDIUM: print

ISSN: 0008-5472

RECORD TYPE: Abstract
LANGUAGE: English

- end of record -

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Display 8/3/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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14062690 BIOSIS NO.: 200300056719
Enhancement of vascular targeting by inhibitors of **nitric oxide synthase**.
AUTHOR: Davis Peter D(a); Tozer Gillian M; Naylor Matthew A; Thomson Peter;
Lewis Gemma; Hill Sally A
AUTHOR ADDRESS: (a)Magdalen Centre, Angiogene Pharmaceuticals Ltd., Oxford
Science Park, Oxford, OX4 4GA, UK**UK E-Mail: pdd@angiogene.co.uk
JOURNAL: International Journal of Radiation Oncology Biology Physics 54 (5
MEDIUM: print
ISSN: 0360-3016
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

- end of record -

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Display 8/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

13793277 BIOSIS NO.: 200200422098
Targeted delivery of agents designed to manipulate **nitric oxide** production in tumours.
AUTHOR: Everett Steven A(a); Moody Christopher J; Naylor Matthew A(a);
Wardman Peter(a)
AUTHOR ADDRESS: (a)Gray Cancer Institute, Mount Vernon Hospital, Northwood,
PO Box 100, Middlesex, HA6 2JR**UK
JOURNAL: Nitric Oxide 6 (4):p383-384 June, 2002
MEDIUM: print
CONFERENCE/MEETING: Second International Conference on Biology, Chemistry
and Therapeutic Applications Prague, Czech Republic June 16-20, 2002
ISSN: 1089-8603
RECORD TYPE: Citation
LANGUAGE: English

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Display 8/3/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

13409512 BIOSIS NO.: 200200038333
Tumor **nitric oxide** levels and vascular targeting with **combretastatin A-4-P**.
AUTHOR: Tozer Gillian Mary(a); Prise Vivien Elaine(a); Wilson Ian(a)
AUTHOR ADDRESS: (a)Gray Laboratory Cancer Research Trust, Middlesex**UK
JOURNAL: Proceedings of the American Association for Cancer Research Annual
Meeting 42p824 March, 2001
MEDIUM: print
CONFERENCE/MEETING: 92nd Annual Meeting of the American Association for
Cancer Research New Orleans, LA, USA March 24-28, 2001
ISSN: 0197-016X
RECORD TYPE: Citation

LANGUAGE: English

- end of record -

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Display 8/3/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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13244597 BIOSIS NO.: 200100451746

Mechanisms associated with tumor vascular shut-down induced by
combretastatin A-4 phosphate: Intravital microscopy and measurement
of vascular permeability.

AUTHOR: Tozer Gillian M(a); Prise Vivien E; Wilson John; Cemazar Maja; Shan
Siqing; Dewhirst Mark W; Barber Paul R; Vojnovic Borivoj; Chaplin David J

AUTHOR ADDRESS: (a)Gray Cancer Institute, Mount Vernon Hospital, Northwood,
Middlesex, HA6 2JR: tozer@graylab.ac.uk**UK

JOURNAL: Cancer Research 61 (17):p6413-6422 September 1, 2001

MEDIUM: print

ISSN: 0008-5472

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

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Display 8/3/6 (Item 6 from file: 5)
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12676397 BIOSIS NO.: 200000429899

Determinants of anti-vascular action by **combretastatin A-4** phosphate:
Role of **nitric oxide**.

AUTHOR: Parkins C S(a); Holder A L; Hill S A; Chaplin D J; Tozer G M

AUTHOR ADDRESS: (a)Tumour Microcirculation Group, Gray Laboratory Cancer
Research Trust, Mount Vernon Hospital, Northwood, Middlesex, HA6 2JR**UK

JOURNAL: British Journal of Cancer 83 (6):p811-816 September, 2000

MEDIUM: print

ISSN: 0007-0920

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

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Display 8/3/7 (Item 7 from file: 5)
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11972059 BIOSIS NO.: 199900225372

Combretastatin A-4 phosphate as a tumor vascular-targeting agent:
Early effects in tumors and normal tissues.

AUTHOR: Tozer Gillian M(a); Prise Vivien E; Wilson John; Locke Rosalind J;
Vojnovic Borivoj; Stratford Michael R L; Dennis Madeleine F; Chaplin
David J

AUTHOR ADDRESS: (a)Tumor Microcirculation Group, Gray Laboratory Cancer
Research Trust, Mount Vernon Hospital, Nort**UK

JOURNAL: Cancer Research 59 (7):p1626-1634 April 1, 1999

ISSN: 0008-5472

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

- end of record -

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Display 8/3/8 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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10178633 Genuine Article#: 491RE No. References: 0
Title: Enhancement of **combretastatin A4** phosphate activity by
nitric oxide synthase inhibitors of different
structural classes.

Author(s): Davis PD; Thomson P; Naylor MA; Nolan J; Lewis GS; Hill SA
Corporate Source: Angiogene Pharmaceut Ltd,Aston Rowant//England//; Gray Lab
Canc Res Trust,Northwood/Middx/England/
Journal: CLINICAL CANCER RESEARCH, 2001, V7, N11,S (NOV), P3656S-3656S
ISSN: 1078-0432 Publication date: 20011100
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202
USA

Language: English Document Type: MEETING ABSTRACT

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Display 8/3/9 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

11644711 EMBASE No: 2002216312
Small-molecule, tubulin-binding compounds as vascular targeting agents
Marx M.A.
Dr. M.A. Marx, Pfizer Global Research/Development, Pfizer Corporation,
Eastern Point Road, Groton, CT 06340 United States
Expert Opinion on Therapeutic Patents (EXPERT OPIN. THER. PAT.) (United
Kingdom) 2002, 12/6 (769-776)
CODEN: EOTPE ISSN: 1354-3776
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 38

- end of record -

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Display 8/3/10 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

11610615 EMBASE No: 2002182701
Angiogenesis: From the molecular mechanisms to the development of new
drugs
Morbidelli L.; Donnini S.; D'Amore V.; Ziche M.
L. Morbidelli, Istituto di Scienze Farmacologiche, Universita di Siena,
Siena Italy
Acta Medica Romana (ACTA MED. ROM.) (Italy) 2001, 39/2 (238-246)
CODEN: AMROB ISSN: 0001-6098
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH; ITALIAN
NUMBER OF REFERENCES: 24

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Display 8/9/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

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12676397 BIOSIS NO.: 200000429899

Determinants of anti-vascular action by **combretastatin A-4 phosphate: Role of nitric oxide.**

AUTHOR: Parkins C S(a); Holder A L; Hill S A; Chaplin D J; Tozer G M

AUTHOR ADDRESS: (a)Tumour Microcirculation Group, Gray Laboratory Cancer Research Trust, Mount Vernon Hospital, Northwood, Middlesex, HA6 2JR**UK

JOURNAL: British Journal of Cancer 83 (6):p811-816 September, 2000

MEDIUM: print

ISSN: 0007-0920

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: The anti-vascular action of the tubulin binding agent **combretastatin A-4 phosphate (CA-4-P)** has been quantified in two

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types of murine tumour, the breast adenocarcinoma CaNT and the round cell sarcoma SaS. The functional vascular volume, assessed using a fluorescent carbocyanine dye, was significantly reduced at 18 h after CA-4-P treatment in both tumour types, although the degree of reduction was very different in the two tumours. The SaS tumour, which has a higher **nitric oxide synthase (NOS)** activity than the CaNT tumour, showed apprx10-fold greater resistance to vascular damage by CA-4-P. This is consistent with our previous findings, which showed that NO exerts a protective action against this drug. Simultaneous administration of CA-4-P with a NOS inhibitor, Nomega-nitro-L-arginine (L-NNA), resulted in enhanced vascular damage and cytotoxicity in both tumour types. Administration of diethylamine NO, an NO donor, conferred protection against the vascular damaging effects. Following treatment with CA-4-P, neutrophil infiltration into the tumours, measured by myeloperoxidase (MPO) activity, was significantly increased. Levels of MPO activity also correlated with the levels of vascular injury and cytotoxicity measured in both tumour types. Neutrophilic MPO generates

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free radicals and may therefore contribute to the vascular damage associated with CA-4-P treatment. MPO activity was significantly increased in the presence of L-NNA, suggesting that the protective effect of NO against CA-4-P-induced vascular injury may be, at least partially, mediated by limiting neutrophil infiltration. The data are consistent with the hypothesis that neutrophil action contributes to vascular injury by CA-4-P and that NO generation acts to protect the tumour vasculature against CA4-P-induced injury. The protective effect of NO is probably associated with an anti-neutrophil action.

REGISTRY NUMBERS: 10102-43-9: **NITRIC OXIDE**; 125978-95-2:

NITRIC OXIDE SYNTHASE

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Cardiovascular System (Transport and Circulation); Tumor Biology

BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata,

Animalia

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DIALOG(R)File 5:Biosis Previews(R)
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ORGANISMS: CaNT cell line (Muridae)--murine breast adenocarcinoma cells;
SaS cell line (Muridae)--murine round sarcoma cells
ORGANISMS: PARTS ETC: neutrophils--blood and lymphatics, immune system,
infiltration
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals;
Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: N-omega-nitro-L-arginine;
combretastatin A-4 phosphate {CA-4-P}--anti-vascular action,
tubulin binding agent; **nitric oxide**; **nitric
oxide synthase**
MISCELLANEOUS TERMS: cytotoxicity; vascular damage
CONCEPT CODES:
34502 Immunology and Immunochemistry-General; Methods
02506 Cytology and Cytochemistry-Animal
10060 Biochemical Studies-General
10802 Enzymes-General and Comparative Studies; Coenzymes
14504 Cardiovascular System-Physiology and Biochemistry

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DIALOG(R)File 5:Biosis Previews(R)
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15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph
Studies
15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies
24003 Neoplasms and Neoplastic Agents-Immunology
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects;
Systemic Effects
34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology
BIOSYSTEMATIC CODES:
86375 Muridae

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Ref	Items	Index-term
E1	2	AU=PERO RON W
E2	4	*AU=PERO RONALD
E3	62	AU=PERO RONALD W
E4	2	AU=PERO RS
E5	1	AU=PERO RT
E6	211	AU=PERO RW
E7	2	AU=PERO S
E8	14	AU=PERO S C
E9	7	AU=PERO S.C.
E10	9	AU=PERO SC
E11	12	AU=PERO SILVA A
E12	1	AU=PERO SILVA A.

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Ref	Items	Index-term
E1	1	AU=PERO, RON W.
E2	8	*AU=PERO, RONALD

E3 2 AU=PERO, RONALD W
E4 124 AU=PERO, RONALD W.
E5 1 AU=PERO, RONALD WILLIAM
E6 1 AU=PERO, RW
E7 1 AU=PERO, S. C.
E8 4 AU=PERO, STEPHANIE C.
E9 1 AU=PERO, SUZANNE FRITTS
E10 1 AU=PEROBA CEN
E11 1 AU=PEROBA M A B
E12 1 AU=PEROBA M.A.B.

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? s e4 and combretastatin

124 AU=PERO, RONALD W.
1835 COMBRETASTATIN
S9 0 AU='PERO, RONALD W.' AND COMBRETASTATIN

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